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In re United States Patent Application of:

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Maria Joao, et al.

Application No.: 10/574,875

Date Filed: April 6, 2006

Title: COMPOUNDS FOR THE
TREATMENT OF DISEASES
ASSOCIATED WITH THE
FORMATION OF AMYLOID
FIBRILS

Docket No.: 4258-120

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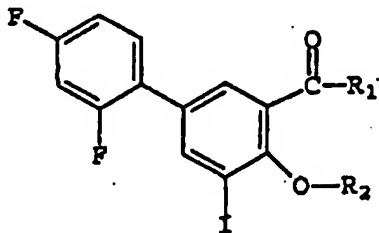
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Via facsimile To Examiner S. Kumar
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PROPOSED AMENDMENT OF CLAIMS

Please cancel claims 7-9, and amend claims 2-6, in the following listing of claims 1-9 of the application:

1. (Original) A compound of structural formula (I):



(I)

in which

R_1 is a $-NR_3R_5$ group, where R_3 and R_5 , independently, are a hydrogen atom or a C_1-C_6 alkyl group; $-OR_C$ group, where R_C is a hydrogen atom or a C_1-C_6 alkyl group; a glycosyl; a C_1-C_6 polyhydroxyalkyl; or a $-NH-CH(R_4)-COOR_6$ group, where R_4 is a

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side chain of one of the 20 natural alpha-amino acids in either of their two enantiomerically pure forms L or D, and R_e is a hydrogen atom or a C_1 - C_6 alkyl group; and

R_2 is a hydrogen atom, a C_1 - C_6 alkyl group, a glycosyl; a C_1 - C_6 polyhydroxyalkyl; $-C(=O)-R_f$ group, where R_f is a C_1 - C_6 alkyl group; or a $-CH_2-COO-R_g$ group, where R_g is a hydrogen atom or a C_1 - C_6 alkyl group;

and pharmaceutically acceptable salts thereof.

2. (Currently amended) A compound according to claim 1, ~~characterised in that~~ wherein R_1 is selected from: OH, NH_2 , OMe, OEt, or a $CH(R_d)-COR_e$ group, where R_d is the side chain of glycine, alanine, leucine, valine, aspartic acid or asparagine and where R_e is H or a C_1 - C_6 alkyl group; and R_2 is selected from: H, Me, glycosyl, a $-C(=O)-R_f$ group, where R_f is a Me, Et, t-Bu group; or a $-CH_2-COO-R_g$ group, where R_g is a hydrogen atom or a t-Bu group.

3. (Currently amended) A compound according to claim 1, ~~characterised in that it is selected from the following compounds~~ group consisting of:

- [1] 5-(2,4-difluorophenyl)-3-iodo-salicylic acid;
- [2] ethyl 5-(2,4-difluorophenyl)-3-iodo-salicylate;
- [3] methyl 5-(2,4-difluorophenyl)-3-iodo-salicylate;
- [4] 5-(2,4-difluorophenyl)-3-iodo-salicylamide;
- [5] tert-butyl [2-aminocarbonyl-4-(2,4-difluorophenyl)-6-iodo-phenoxy]-acetate;
- [6] [2-aminocarbonyl-4-(2,4-difluorophenyl)-6-iodo-phenoxy]acetic acid;
- [7] 5-(2,4-difluorophenyl)-3-iodo-salicylic acid 1-O- β -glycoside;
- [8] ethyl 2',4'-difluoro-4-methoxy-5-iodo-[1,1']biphenyl-3-carboxylate;
- [9] 2',4'-difluoro-4-methoxy-5-iodo-[1,1']biphenyl-3-carboxylic acid;
- [10] ethyl 2',4'-difluoro-4-acetyloxy-5-iodo-[1,1']biphenyl-3-carboxylate;
- [11] 2',4'-difluoro-4-(*t*-butylcarbonyloxy)-5-iodo-[1,1']biphenyl-3-carboxylic acid;
- [12] 2',4'-difluoro-4-(ethylcarbonyloxy)-5-iodo-[1,1']biphenyl-3-carboxylic acid;
- [13] ethyl ester of N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]glycine;
- [14] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]glycine;
- [15] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]alanine;
- [16] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]leucine;
- [17] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]serine;

- [18] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]valine;
[19] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]-aspartic acid; and
[20] N-[5-(2,4-difluorophenyl)-3-iodo-salicyloyl]asparagine.

4. (Currently amended) A method for the preparation of a compound of formula (I) according to ~~claims claim 1, characterised in that it comprises~~ comprising a step of reacting diflunisal or at least one derivatives derivative thereof with an iodination reagent.

5. (Currently amended) A method according to claim 4, ~~characterised in that~~ wherein the iodination reagent ~~may be selected from~~ is selected from the group consisting of: elemental iodine; iodide salts; ~~such as~~ sodium iodide; ~~or~~ potassium iodide; iodonium salts; ~~such as~~ iodine chloride; iodonium complexes; ~~such as~~ bis(pyridine)iodonium (I) tetrafluoroborate; ~~or~~ bis(sym-collidine)iodonium (I) hexafluorophosphate; ~~and~~ organic iodine compounds; ~~such as~~ iodobenzene diacetate; and ~~or~~ N-iodosuccinimide.

6. (Currently amended) A pharmaceutical composition containing a compound according to ~~claims claim 1,~~ and one or more pharmaceutically acceptable excipients.

7.-9. (Canceled)

REMARKS

By the above amendments, claims 2-6 have been placed in form for allowance and issue.

Claim 5 has been amended to set forth the selection species in Markush-type format.

The selection group in claim 5 is properly constituted. See MPEP 2173.05 (h), which provides that

"... the double inclusion of an element by members of a Markush group is not, in itself, sufficient basis for objection to or rejection of claims.... The mere fact that a compound may be embraced by more than one member of a Markush group recited in the claim does not necessarily render the scope of the claim unclear. For example, the Markush group, "selected from the group consisting

of amino, halogen, nitro, chloro and alkyl" should be acceptable even though "halogen" is generic to 'chloro.'"

Accordingly, all claims 1-6, as herein amended, are now in condition for allowance.

Respectfully submitted,



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